ENVIRON

Comments to the NTP's Board of Scientific Counselors
Formaldehyde

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1. My presence here is supported by Hexion Specialty Chemicals, Inc., a manufacturer of formaldehyde. My comments are directed entirely to the question of whether the NTP has clearly established, based on well-accepted and explicitly stated scientific criteria, that there is a causal link between exposure to formaldehyde and myeloid leukemia in humans.

2. The draft Substance Profile conclusion, that formaldehyde is known to be a human carcinogen, is said to be based on epidemiological studies providing "consistent findings of nasopharyngeal cancer, sinonasal cancer, and myeloid leukemia." This evidence is said to be further supported by studies on mechanisms of carcinogenesis.

3. I suggest that if you examine carefully all of the evidence related specifically to myeloid leukemia, and then apply the usual criteria used to examine questions of causality, you would conclude that formaldehyde cannot be said to be causally related to leukemia. The draft Substance Profile assertion that there is a consistent pattern of strong associations observed in the epidemiology studies is not supported by a thorough examination of all of the available literature. The draft apparently ignores the fact that there is a lack of statistical significance in most studies, and no consistent associations between risk and the measure of exposure. The draft also discounted the Bachand et al. (2010) meta-analysis because it did not include results from studies that relied on proportional mortality rates (PMRs); the latter are generally considered as hypothesis-generating studies, and were excluded for reasons well described by Bachand et al. The attached Figure, from the Bachand et al. meta-analysis, illustrates my points.

4. Moreover, the few associations seen in the human findings are not strengthened by the available experimental evidence. Rather, at its most elementary level, the experimental evidence strongly suggests that formaldehyde exposure does not reach and produce damage at any sites, including bone marrow, that are distant from the portal of entry. It is difficult to see how a compound with this behavior could induce leukemia.

5. My colleagues and I have submitted detailed comments on this matter, and do not believe that those comments (as well as those of others) have been adequately addressed by the NTP.

6. Note that the NTP's classification of formaldehyde as "known to be a human carcinogen" would remain correct even if it were to be concluded that the evidence did not support classification of formaldehyde as a cause of human leukemia, as long as causality were said to be established for either of the nasal cancers.

7. I urge the BSC to advise the NTP to examine the evidence for formaldehyde's association with myeloid leukemia and to determine, using explicitly stated criteria for causality, whether and how a causal claim can be established for this disease. The scientific evidence related to this disease is very different from that related to the nasal tumors, and I suggest much confusion will ensue unless the lines of reasoning leading to a conclusion about leukemia causation, or lack thereof, are fully elaborated.

8. A Committee of the National Academy of Sciences has just begun an independent review of EPA's draft assessment of formaldehyde's health risks, and, among others, will be examining the question of formaldehyde's relationship to leukemia. I suggest the NTP consider putting aside a decision on this question until the NAS panel publishes its conclusions. Not only might NTP benefit from the work of this expert panel, but achieving government-wide consistency on this question will also be highly beneficial.

Thank you.

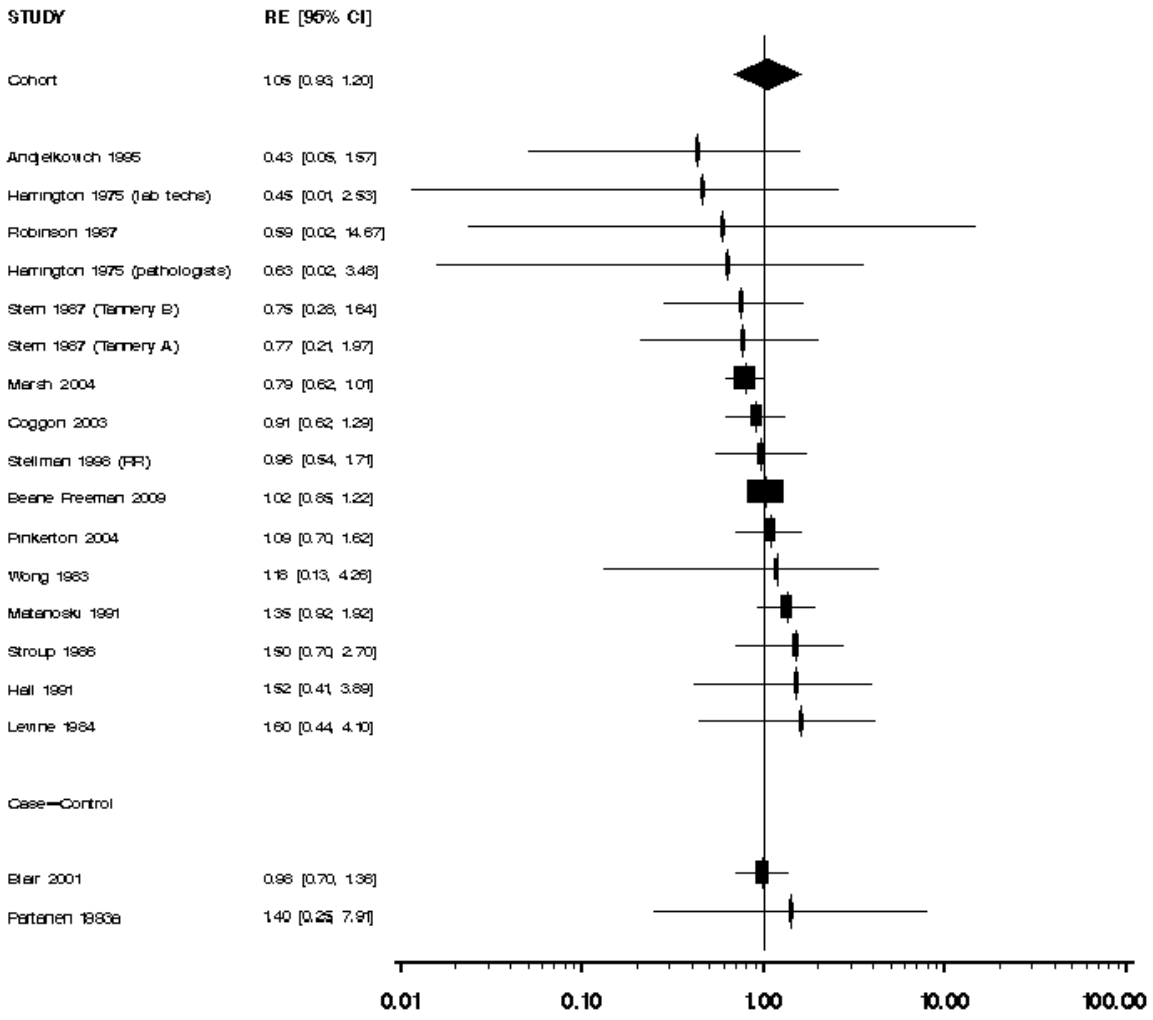

Figure 1: Forest plot by study design for leukemia

From: Bachand AM, Mundt KA, Mundt DJ, Montgomery RR. 2010. Epidemiological studies of formaldehyde exposure and risk of leukemia and nasopharyngeal cancer: a meta-analysis. Crit Rev Toxicol; 40(2):85-100.